

Amendments to the Claims

Listing of Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (Currently Amended) A crystal of the Liver X receptor beta ligand binding domain (LXR β LBD) selected from the group consisting of:

(a) a crystal complex of LXR β LBD bound to N-(2,2,2-trifluoroethyl)-N-[4[2,2,2-trifluoro-1-hydroxy-1-(trifluoromethyl)ethyl]phenyl]-benzenesulfonamide, said crystal complex belonging to space group P2₁2₁2₁, wherein said LXR β LBD consists essentially of the amino acid sequence from Leu220 to Glu461 or Gly213 to Glu461 of [a] the human LXR β as set forth in SEQ ID NO:1; shown in Figure 5a (SEQ ID NO: 1); and

(b) a crystal complex of LXR β LBD bound to 3-(3-(2-chloro-3-trifluoromethylbenzyl)-2,2-diphenylethylamino)propoxy)phenylacetic acid, said crystal complex belonging to space group P2₁2₁2₁, wherein said LXR β LBD comprises the amino acid sequence from Leu220 to Glu461 or Gly213 to Glu461 of the human LXR β as set forth in SEQ ID NO:1;

[(b)] (c) a crystal complex of LXR β LBD bound to N-(2,2,2-trifluoroethyl)-N-[4[2,2,2-trifluoro-1-hydroxy-1-(trifluoromethyl)ethyl]phenyl]-benzenesulfonamide, said crystal complex belonging to space group P6₁22, wherein said LXR β LBD comprises the amino acid sequence from Leu220 to Glu461 of [a] the human LXR β as set forth in SEQ ID NO:1;

(d) a crystal of LXR β LBD belonging to space group P6₁22, wherein said LXR β LBD comprises the amino acid sequence from Leu220 to Glu461 of the human LXR β as set forth in SEQ ID NO:1; and

(e) a crystal complex of LXR β LBD bound to a coactivator peptide Nuclear Receptor (NR) box 1 of Transcription Intermediary Factor 2 (TIF2), said crystal complex belonging to space group P2₁2₁2₁, wherein said LXR β LBD comprises the amino acid sequence from Leu220 to Glu461 or Gly213 to Glu461 of the human LXR β as set forth in SEQ ID NO:1, shown in Figure 5a (SEQ ID NO: 1), or a polypeptide comprising an amino acid sequence at least 95% identical to the sequence from Leu220 to Glu461 of human LXR β (SEQ ID NO:1), wherein said

polypeptide is capable of binding ~~complexed~~ to an LXR β ligand, said LXR β ligand being chosen from N-(2,2,2-trifluoroethyl)-N-[4(2,2,2-trifluoro-1-hydroxy-1-(trifluoromethyl)ethyl)phenyl]-benzenesulfonamide, 3-(3-(2-chloro-3-trifluoromethylbenzyl-2,2-diphenylethylamino)propoxy)phenylacetic acid, 24(S),25-epoxycholesterol, or N-[1-(2-furanyl)ethyl]-N-4-pyridinyl-tricyclo[3.3.1.1^{3,7}]decane-1-carboxamide.

2. (Currently Amended) The crystal according to claim 1, wherein the LXR β LBD in the crystal belonging to space group P6₁22, P2₁2₁2₁ or P2₁2₁2 ~~comprises~~ consists of the amino acid sequence from Leu220 to Glu461 of a human LXR β as set forth in SEQ ID NO:1 shown in Figure 5a (SEQ ID NO: 1).

3. (Currently Amended) The crystal according to claim 1 or 2, wherein the crystal complex (a) has space group P2₁2₁2₁ and has unit cell dimensions a = 58.7 Å, b = 103.3 Å, c = 176 Å, further comprising N-(2,2,2-trifluoroethyl)-N-[4(2,2,2-trifluoro-1-hydroxy-1-(trifluoromethyl)ethyl)phenyl]-benzenesulfonamide bound to the LXR β LBD.

4. (Currently Amended) The crystal according to claim 1 or 2[3], wherein said crystal complex (b) ~~has belongs to~~ space group P2₁2₁2₁ and has the unit cell dimensions a = 58.7 Å, b = 98.9 Å, c = 175.8 Å, a = 59 +/- 3 Å, b = 100 +/- 5 Å, c = 176 +/- 3 Å, or a = 58.7 Å, b = 103.3 Å, c = 176 Å, wherein $\alpha = \beta = \gamma = 90^\circ$.

5. (Currently Amended) The crystal according to claim 1 or 2[3], wherein said crystal complex (c) ~~belongs to~~ has space group P6₁22 and has the unit cell dimensions a = b = 58.7 Å, c = 293.8 Å, $\alpha = \beta = 90^\circ$, $\gamma = 120^\circ$.

6. (Currently Amended) The crystal according to claim 1 or 2[3], wherein the crystal complex (e) has space group P2₁2₁2 and has unit cell dimensions a = 89 +/- 3 Å, b = 91 +/- 3 Å, c = 131 +/- 3 Å, $\alpha = \beta = \gamma = 90^\circ$, further comprising 3-(3-(2-chloro-3-trifluoromethylbenzyl-2,2-diphenylethylamino)propoxy)phenylacetic acid bound to the LXR β LBD.

7. (Currently Amended) The crystal according to claim 1 or 2, 6; wherein said crystal (d) has belongs to space group $P6_122$ and has the unit cell dimensions $a = 59 \pm 3 \text{ \AA}$, $b = 59 \pm 3 \text{ \AA}$, $c = 294 \pm 3 \text{ \AA}$, ~~or~~ $a = 58.7 \text{ \AA}$, $b = 98.9 \text{ \AA}$, $c = 175.8 \text{ \AA}$, wherein $\alpha = \beta = 90^\circ$, $\gamma = 120^\circ$.

8. (Currently Amended) A crystal of the Liver X receptor beta ligand binding domain (LXR β LBD) belonging to the space group $P2_12_12_1$ and having the unit cell dimensions $a = 59 \pm 3 \text{ \AA}$, $b = 100 \pm 5 \text{ \AA}$, $c = 176 \pm 3 \text{ \AA}$, $\alpha = \beta = \gamma = 90^\circ$.

9. (Previously Presented) A crystal of Liver X receptor beta ligand binding domain (LXR β LBD) belonging to the space group $P6_122$ and having the unit cell dimensions $a = 59 \pm 3 \text{ \AA}$, $b = 59 \pm 3 \text{ \AA}$, $c = 294 \pm 3 \text{ \AA}$, $\alpha = \beta = 90^\circ$, $\gamma = 120^\circ$.

10. (Currently Amended) A crystal of Liver X receptor beta ligand binding domain (LXR β LBD) in complex with a coactivator peptide Nuclear Receptor (NR) box 1 of Transcription Intermediary Factor 2 (TIF2) (~~NR box 1 of TIF2~~) belonging to the space group $P2_12_12_1$ and having the unit cell dimensions $a = 89 \pm 3 \text{ \AA}$, $b = 91 \pm 3 \text{ \AA}$, $c = 131 \pm 3 \text{ \AA}$, $\alpha = \beta = \gamma = 90^\circ$.

11. (Currently amended) A crystal according to any of claims 8-10, ~~claim 1~~, having a resolution determined by X-ray crystallography of better than 3.6 \AA .

12. (Original) A crystal according to claim 11 having a resolution determined by X-ray crystallography of better than 2.9 \AA .

13. – 28. (Canceled)

29. (Currently Amended) A crystallized molecule or molecular complex comprising a binding pocket defined by the structural coordinates of human Liver X receptor beta ligand binding domain (LXR β LBD) comprising amino acid residues Ser242, Phe268, Phe271, Thr272 ~~Thr272~~, Leu274, Ala275, Ser278, Ile309, Met312, Leu313, Glu315, Thr316, Arg319, Ile327,

Phe329, Leu330, Tyr335, Phe340, Leu345, Phe349, Ile350, Ile353, Phe354, His435, Gln438, ~~Val439~~ ~~Val439~~, Leu442, Leu449, Leu453, and Trp457, according to the structural coordinates of the complex of LXR β LBD and 3-(3-(2-chloro-3-trifluoromethylbenzyl-2,2-diphenylethylamino)propoxy)phenylacetic acid ~~3-(3-(2-chloro-3-trifluoromethylbenzyl-2,2-diphenylethylamino)propoxy)phenylacetic acid~~ as shown in Table 2, ~~or a homologue of said molecule or molecular complex wherein said homologue has~~ or having a root mean square deviation ~~from~~ ~~from~~ the backbone atoms of said amino acids of not more than 1.5 Å, wherein said LXR β LBD consists of the amino acid sequence from Leu220 to Glu461 or Gly213 to Glu461 of the human LXR β as set forth in SEQ ID NO:1.

30. (Currently Amended) A crystallized molecule or molecular complex comprising a binding pocket defined by the structural coordinates of human Liver X receptor beta ligand-binding domain (LXR β LBD) comprising amino acid residues Ser242, Phe268, Phe271, Thr272 ~~Thr272~~, Leu274, Ala275, Ser278, Ile309, Met312, Leu313, Glu315, Thr316, Arg319, Ile327, Phe329, Leu330, Tyr335, Phe340, Leu345, Phe349, Ile350, Ile353, Phe354, His435, Gln438, Val439 ~~Val439~~, Leu442, Leu449, Leu453, and Trp457, according to the complex LXR β LBD and N-(2,2,2-trifluoroethyl)-N-[4[2,2,2-trifluoro-1-hydroxy-1-(trifluoromethyl)ethyl]phenyl]-benzenesulfonamide as shown in Table 2, ~~or a homologue of said molecule or molecular complex having~~ a root mean square deviation ~~from~~ ~~from~~ the backbone atoms of said amino acids of not more than 1.5 Å, wherein said LXR β LBD consists of the amino acid sequence from Leu220 to Glu461 or Gly213 to Glu461 of the human LXR β as set forth in SEQ ID NO:1.

31. (Currently Amended) An isolated protein consisting ~~essentially of~~ the amino acid sequence shown from amino acid 220 to amino acid 461 as set forth in SEQ ID NO:1 ~~in Figure 5a (SEQ ID NO: 1)~~ or the sequence shown as set forth in SEQ ID NO:2 ~~in Figure 5b (SEQ ID NO: 2)~~.

32. (Currently Amended) An isolated protein according to claim 31, additionally comprising ~~a tag, such as a his-tag.~~

33. – 34. (Canceled)

35. (Previously Presented) An isolated protein having an amino acid sequence identical to the amino acid sequence used in a crystal according to claim 1.

36. – 39. (Canceled)

40. (Currently Amended) A crystal of the Liver X receptor beta ligand binding domain (LXR β LBD) in complex with a coactivator peptide Nuclear Receptor (NR) box 1 of Transcription Intermediary Factor 2 (TIF2) (NR-box 1 of TIF2), wherein:

said crystal belongs to space group P2₁2₁2₁; and

said LXR β LBD comprises the amino acid sequence from Leu220 to Glu461 of a human LXR β as set forth in SEQ ID NO:1, shown in Figure 5a (SEQ ID NO: 1), or a polypeptide ~~having an amino acid sequence at least 95% identical to the sequence from Leu220 to Glu461 of a human LXR β (SEQ ID NO:1), wherein said polypeptide is capable of binding to an LXR β ligand, said LXR β ligand being chosen from N-(2,2,2-trifluoroethyl)-N-[4(2,2,2-trifluoro-1-hydroxy-1-(trifluoromethyl)ethyl]phenyl]-benzenesulfonamide, 3-(3-(2-chloro-3-trifluoromethylbenzyl-2,2-diphenylethylamino)propoxy)phenylacetic acid, 24(S),25-epoxycholesterol, or N-[1-(2-furanyl)ethyl]-N-4-pyridinyl-tricyclo[3.3.1.1.3,7]decane-1-carboxamide Liver-X-receptor-beta-ligand-binding-domain (LXR β -LBD).~~

41. (Currently Amended) The crystal of LXR β LBD of claim 40, wherein the LXR β LBD consists of ~~comprises~~ the amino acid sequence from Leu220 to Glu461 of a human LXR β as set forth in SEQ ID NO:1 shown in Figure 5a (SEQ ID NO: 1).

42. (Currently Amended) The crystal of LXR β LBD of claim 41, said crystal having space group P2₁2₁2₁ and having the unit cell dimensions $a = 89 \pm 3 \text{ \AA}$, $b = 91 \pm 3 \text{ \AA}$, $c = 131 \pm 3 \text{ \AA}$, $\alpha = \beta = \gamma = 90^\circ$.

43. (Currently Amended) The crystallized molecule or molecular complex of claim 29 or 30, wherein the structural coordinates of said binding pocket were was-resolved by molecular replacements using the structure of a thyroid hormone receptor as a search model.

44. (Currently Amended) The crystallized molecule or molecular complex of claim 29, wherein the complex of LXR β LBD and 3-(3-(2-chloro-3-trifluoromethylbenzyl-2,2-diphenylethylamino)propoxy)phenylacetic acid ~~3-(3-(2-chloro-3-trifluoromethylbenzyl-2,2-diphenylethylamino)propoxy)phenylacetic acid~~ has the structural coordinates according to Table 2, or a ~~homologue of said molecule or molecular complex~~ having a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5 Å.

45. (Currently Amended) The crystallized molecule or molecular complex of claim 30, wherein the complex of LXR β LBD and N-(2,2,2-trifluoroethyl)-N-[4[2,2,2-trifluoro-1-hydroxy-1-(trifluoromethyl)ethyl]phenyl]-benzenesulfonamide has the structural coordinates according to Table 2, or a ~~homologue of said molecule or molecular complex~~ having a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5 Å.